Behavioral Outcomes and Evidence of Psychopathology Among Very Low Birth Weight Infants at Age 20 Years

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ABSTRACT. *Objective.* Information on the mental health of very low birth weight (VLBW; <1500 g) children in young adulthood is sparse. We thus sought to examine gender-specific behavioral outcomes and evidence of psychopathology in a cohort of VLBW young adults at 20 years of age.

Methods. We compared a cohort of 241 survivors among VLBW infants who were born between 1977 and 1979 (mean birth weight: 1180 g; mean gestational age at birth: 29.7 weeks), 116 of whom were men and 125 of whom were women, with 233 control subjects from the same population in Cleveland who had normal birth weights (108 men and 124 women). Young adult behavior was assessed at 20 years of age with the Achenbach Young Adult Self-Report and the Young Adult Behavior Checklist for parents. In addition, the young adults and parents completed the ADHD Rating Scale for Adults. Gender-specific outcomes were adjusted for sociodemographic status.

Results. VLBW men reported having significantly fewer delinquent behaviors than normal birth weight (NBW) control subjects, but there were no differences on the Internalizing, Externalizing, or Total Problem Behavior scales. Parents of VLBW men reported significantly more thought problems for their sons than did parents of control subjects. VLBW women reported significantly more withdrawn behaviors and fewer delinquent behavior problems than control subjects. Their rates of internalizing behaviors (which includes anxious/depressed and withdrawn behaviors) above the borderline clinical cutoff were 30% versus 16% (odds ratio: 2.2; 95% confidence interval [CI]: 1.2-4.1). Parents of VLBW women reported significantly higher scores for their daughters on the anxious/depressed, withdrawn, and attention problem subscales compared with control parents. The odds ratios for parent-reported rates above the borderline-clinical cutoff among women for the anxious/depressed subscale was 4.4 (95% CI: 1.4-13.5), for thought problems was 3.7 (95% CI: 1.2-11.6), and for attention problems was 2.4 (95% CI: 1.0-5.5). There were no differences in the young adult self-report of attention-deficit/hyperactivity disorder (ADHD). Parents of VLBW men reported higher mean scores on the attention subtype of ADHD but not higher rates of ADHD.

Conclusion. The increase in psychopathology among VLBW survivors in young adulthood indicates a need for anticipatory guidance and early intervention that might help to prevent or ameliorate potential psychopathology. *Pediatrics* 2004;114:932–940; *very low birth weight, psychopathology, behavior.*

Reports of the young adult outcomes of very low birth weight (VLBW; <1.5 kg) children who survived the initial years of neonatal intensive care reveal that the neurodevelopmental sequelae and poor educational achievement evident during childhood persist into adulthood.[1,2] There is, however, very little information concerning the behavior and mental health of VLBW children who reach adulthood.[3]

Epidemiologic studies suggest an association between perinatal risk and psychiatric disorder, including schizophrenia,[4] affective disorder,[5–7] and antisocial behavior.[8,9] Perinatal risk factors identified in these studies, which also co-occur among VLBW populations, include maternal undernutrition,[10,11] low birth weight,[11,12] low gestation,[7,12] small head circumference,[12,13] and asphyxia.[14] Childhood risk factors for the development of adult psychopathology that are also seen among VLBW children include intellectual disability,[15,16] neurologic problems,[17,18] poor physical health,[19] and chronic illness.[20,21]

During childhood and adolescence, VLBW children are reported to have more overall behavioral problems compared with normal birth weight (NBW) control subjects.[22] These include both internalizing and externalizing symptoms.[23,24] The most common problems are attentional weaknesses and hyperactivity,[23–28] although a pattern of shyness and withdrawn behavior has also been described,[29,30] as well as anxiety and depression[23,25,31] and poor social skills.[32] The extent to which these problems persist into adulthood is unknown.

As part of a longitudinal study, we sought to examine gender-specific behavioral outcomes and evidence of psychopathology among a cohort of 20-

year-old VLBW young adults. We hypothesized that VLBW young men and women would demonstrate higher rates of behavioral problems and more psychopathology than NBW control subjects.

METHODS

VLBW Group

A cohort of 490 VLBW children were admitted to Rainbow Babies and Children's Hospital (Cleveland, OH) between 1977 and 1979, 312 (64%) of whom survived to 20 years of age.[1] Seventy subjects were not studied at 20 years of age: 58 could not be located, 5 lived out of state, 6 declined to participate, and 1 had severe spastic quadriplegia. The original 20-year study population thus included 242 VLBW participants, 241 of whom (116 men and 125 women) completed the Achenbach Young Adult Self-Report (YASR) of behavior[33] and constitute the study population. They compose 77% of the surviving birth cohort. One parent of 226 (94%) of the study participants was also interviewed and completed the Achenbach Young Adult Behavioral Checklist (YABCL).[33] They compose 72% of parents of the surviving birth cohort. The biological, adoptive, or stepmother was the parent interviewed in 92% of the cases.

The 241 participants had a mean birth weight of 1180 g and were born at a mean gestational age of 29.7 weeks. A description of maternal sociodemographic status at the time of birth, pregnancy risk, infant birth data, neonatal risk, and rehospitalization during infancy is presented in Table 1. VLBW men and women did not differ in their maternal sociodemographic descriptors or birth data; antepartum, intrapartum, or neonatal risk scores[34]; or length of neonatal hospital stay. Significantly more men than women were born at the perinatal center. Men also had higher rates of rehospitalization before 8 months' corrected age than women. The cohort was born before the advent of cerebral ultrasonography; thus, the rates of periventricular hemorrhage and leukomalacia are unknown. There were no major congenital malformations or infections.

The young adult study participants did not differ significantly from those who were not studied in terms of the sociodemographic characteristics of their mothers at the time of their birth; 35 versus 39% of their mothers, respectively, were unmarried; 47% versus 55% were black; and 25% versus 32% had less than a high school education. They differed, however, in the composite sociodemographic risk score: 25% versus 38% of those not studied had a score of 0, 42% versus 23% had a score of 1, 22% versus 27% had a score of 2, and 11% versus 13% had a score of 3, respectively (P = .02). Mean birth weight, gestational age, and rates of neonatal problems did not differ significantly, although more participants than nonparticipants were born at the perinatal center (46 vs 31%; P = .03). Nine percent of the study participants had neurosensory impairments versus 15% for those who were not studied at 20 years of age (not significant). At age 8 years, the mean IQ of the 20-year participants was 96 ± 17 versus 89 ± 23 for those who were not studied at 20 years of age (P = .09), and 5% versus 4% had an IQ <70 (not significant). They did not differ in Internalizing or Externalizing scores on the 8-year Achenbach Child Behavior Checklist (CBCL).

NBW Control Group

The original control group included 366 NBW children who were born at term gestation in 1977, 1978, or 1979 and were selected by means of a population-sampling procedure when they were 8 years of age.[35] Three control subjects died between 8 and 20 years of age. Of the remaining 363 control subjects, 130 were not studied at 20 years of age: 91 could not be located, 1 lived out of state, and 38 declined to participate. The 20-year control population thus included 233 participants, 232 of whom (108 men and 124 women) completed the YASR and are the subjects of this study. They constitute 63% of the cohort that was recruited at 8 years of age. One parent of 217 (94%) of the control subjects was also interviewed and completed the YABCL. The parent interviewed was the biological, adoptive, or stepmother in 95% of cases.

The control subjects who participated at 20 years had significantly higher mean IQ scores at 8 years of age than those who did

TABLE 1. Maternal Demographic Status and Infant Birth, Neonatal, and Infancy Data for Male and Female VLBW Young Adults

	Men (n = 116)	Women (n = 125)
Maternal factors		
Married*	72 (62%)	85 (68%)
Education*		
< High school	32 (28%)	27 (22%)
High school	45 (39%)	56 (45%)
> High school	39 (34%)	42 (34%)
Black race	67 (58%)	65 (52%)
Composite sociodemographic score†		
0	35 (30%)	44 (35%)
1	35 (30%)	38 (30%)
2	39 (34%)	31 (25%)
3	7 (6%)	12 (10%)
Antepartum risk score	10.8 ± 10	9.5 ± 11
Intrapartum risk score	17.1 ± 13	17.1 ± 12
Delivery at perinatal center	63 (54%)	47 (38%)‖
Birth and neonatal data		
Birth weight, mean g ± SD	1193 ± 215	1167 ± 222
Gestational age, mean wk ± SD	29.6 ± 2	29.8 ± 2
SGA‡	22 (19%)	24 (19%)
Multiple birth§	19 (16%)	24 (19%)
Neonatal risk score, median, range	50 (5–180)	45 (5–155)
Days hospital stay, median, range	58 (12–365)	57 (7–456)
Rehospitalization		
Before 8 mo corrected age	48 (41%)	29 (23%)#
Between 8 and 20 mo	16 (14%)	11 (9%)

* At birth.
† In the calculation of this composite score, 1 point was assigned for each of the following factors: unmarried status, black race, and less than a high school education.
‡ < −2 SD.[81]
§ Data are for participants who were born either a twin or, in 1 case, a triplet.
‖ P < 0.05.
# P < 0.01.

not participate at 20 years (105 ± 16 vs 93 ± 15; $P < .001$), and 0.4% versus 5% had a subnormal IQ ($P = .06$). They did not differ in Internalizing or Externalizing scores on the 8-year CBCL. At the children's eighth year, fewer mothers of those who participated at 20 years than of those who did not were unmarried (36% vs 61%; fewer had less than a high school education (11% vs 27%), and fewer were black (55% vs 76%; $P < .001$ for all comparisons). They also differed in the composite sociodemographic risk score: 39% of the participants had a score of 0 compared with 10% of the nonparticipants, 28% versus 32% had a score of 1, 25% versus 43% had a score of 2, and 7% versus 15% had a score of 3, respectively ($P < .001$).

Sociodemographic Status and 20-Year IQ of VLBW and NBW Participants

When the children were 8 years of age, fewer mothers of the VLBW participants than mothers of the NBW control subjects had graduated from high school (83% vs 89%; $P < .05$), although the gender-specific comparisons did not reach statistical significance. The VLBW and control groups did not differ in maternal marital status (59% vs 64% married), race (55% of each group were black), or the composite sociodemographic risk score (33% vs 39% had a score of 0, 30% vs 28% had a score of 1, 29% vs 25% had a score of 2, and 8% vs 7% had a score of 3).[35] The VLBW participants had significantly higher rates of neurosensory impairment (24 [10%] vs 1 [0.4%]) and lower mean 20-year IQ scores than control subjects (88 vs 95 and 86 vs 90 for men and women, respectively; $P < .05$). The rates of subnormal IQ were 7% versus 2% for VLBW and NBW men ($P < .05$) and 5% versus 1% for VLBW and NBW women ($P = .06$).

Measures and Variables

Young adult problem behavior was assessed from the perspective of the young adult via self-administration of the YASR and from that of the parent or adult caregiver via the YABCL. The YASR and YABCL were developed by Achenbach to tap behavior in the transition period between adolescence and adulthood.[33] These questionnaires are designed to provide standardized descriptions of behavior, feelings, thoughts, and competencies rather than diagnoses per se. They include adult analogs or counterparts of items from the CBCL and Youth Self-Report. The YASR has 130 problem items plus 20 competence and social desirability items. Each item is based on the preceding 6 months and is scored on a 3-step scale ranging from 0 to 2, where 0 = not true, 1 = somewhat or sometimes true, and 2 = very often or often true. Additional items concern work, school, marital and other relationships, and substance use. The YABCL has 109 problem items and 11 competence items that are scored on 3-step scales like those of the YASR. Eight syndromes are derived from the items on the YASR and YABCL, including 2 designated as Internalizing (Anxious/Depressed, Withdrawn) and 3 designated as Externalizing (Aggressive, Delinquent, and Intrusive Behavior). Reliability on the YABCL averages 0.85 across syndromes and Internalizing, Externalizing, and Total Problems scales ($P < .001$). Validity has been demonstrated by showing significantly higher scores for subjects referred for mental health services than for matched nonreferred subjects.[36–38] For the 8 syndrome scales, the 95th percentile is considered the borderline clinical cutoff and the 98th percentile the clinical cutoff on the basis of a nonreferred population. For the problem scales (Internalizing, Externalizing, and Total Problems), the 83rd percentile is considered the borderline clinical cutoff and the 90th percentile the clinical cutoff.[33] In the present study, adaptive functioning on the YASR was considered only for the scales designated as Friends and Family as these scales were relevant for all subjects.

The young adults and parents also completed the ADHD Rating Scale for Adults.[39,40] This scale contains 18 items from the diagnostic criteria for attention-deficit/hyperactivity disorder (ADHD) in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). Each item is rated on a scale ranging from 0 to 3 (ranging from "not at all or rarely" to "sometimes," "often," and "very often"). Nine symptoms pertain to inattention, and 9 pertain to hyperactive-impulsive symptoms. The presence of at least 6 of the 9 symptoms rated as "often" or "very often" in each of these categories is considered clinically significant, allowing such subjects to be classified as having the Inattentive, Hyperactive-Impulsive, or combined (Inattentive and Hyperactive Im-

pulsive) subtypes of ADHD. The correlation between young adult self- and parent ratings for current symptoms is $r = 0.76$ ($P < .001$).[40]

Forty-nine percent of the subjects and/or their parents participated in the study at the clinical research center at the hospital; for 50%, the research assistants made home visits, and 1% responded by mail. The young adults and their parents completed the questionnaires via self-administration with the exception of 5% of subjects who were interviewed because of their difficulty in reading. All of the participants and their parents provided written informed consent to participate in the study.

Statistical Analyses

Univariate comparisons between the VLBW and NBW groups were made with the use of t test for continuous variables and with the χ^2 test or Fisher exact test for discrete variables. Logistic regression was used to include covariates of dichotomous outcomes, and multiple linear regression was used for continuous outcomes. Because gender differences in the development of psychopathology occur in the postpubertal years, all outcomes were examined separately for men and women.[33,41,42] Because of the known effects of sociodemographic factors on behavioral outcomes, we controlled for sociodemographic status in the analyses.[43] Birth sociodemographic descriptors were available only for the VLBW subjects. We thus used the mother's marital and educational status at the time the child was 8 years of age for analyses that included the VLBW and control populations. These maternal social status indicators were considered to span the period of childhood and to be more relevant than the mother's social status at 20 years. A composite score representing the mother's sociodemographic status, which we have previously used, was calculated by assigning 1 point for each of the following factors: unmarried status, black race, and less than a high school education.[35] The composite score ranged from 0 to 3. Because of possible effects of IQ on behavioral outcomes,[44] in separate analyses, we controlled for IQ as assessed with the Short Form of the Wechsler Adult Intelligence Scale–Revised.[45]

RESULTS

Comparisons of Behavior on the YASR and YABCL

Comparison of VLBW and NBW Men

VLBW men reported significantly fewer delinquent behaviors than their NBW peers, but the groups did not otherwise differ in terms of problem behaviors or in the overall internalizing, externalizing, or total behavior problems reported (Table 2). The self-reported rates of behavioral disorder above the borderline clinical cutoff did not differ significantly from those of the control subjects (Table 3). On the adaptive scales, VLBW men reported significantly lower scores on excessive alcohol use (days drunk in the past 6 months) than control subjects (mean scores: 7 vs 15; $P < .05$), but they did not differ in their reporting of smoking, drug use, or relationships with friends and family (data not shown).

In contrast to the YASR, parents of VLBW men reported significantly more thought problems for their young adult sons than did parents of control subjects (Table 4). The parent-reported rates of thought disorder and withdrawn behavior above the borderline clinical cutoff were also significantly higher for VLBW men than for control subjects (Table 3).

All of the above described results remained significant after adjusting for 20-year IQ and when subjects with neurosensory impairments were excluded from the analyses, with the exception that in both instances, significantly more VLBW men also had withdrawn behavior on the YABCL ($P < .05$). How-

TABLE 2. Self-Report on Behavioral Outcomes of VLBW and NBW 20-Year-Old Subjects

YASR	Men			Women		
	VLBW (Mean ± SD; n = 116)	NBW (Mean ± SD; n = 108)	Mean Difference* (95% CI)	VLBW (Mean ± SD; n = 125)	NBW (Mean ± SD; n = 124)	Mean Difference* (95% CI)
Anxious/Depressed	7.2 ± 5.3	8.4 ± 6.4	−1.4 (−2.9 to 0.2)	10.2 ± 7.3	9.2 ± 6.4	1.0 (−0.7 to 2.8)
Withdrawn	3.4 ± 2.5	3.3 ± 2.4	0.0 (−0.6 to 0.6)	3.9 ± 2.6	3.0 ± 2.2	0.8 (0.2 to 1.4)†
Somatic Complaints	2.8 ± 2.9	2.9 ± 2.7	−0.2 (−0.9 to 0.6)	4.3 ± 3.8	4.0 ± 3.5	0.3 (−0.6 to 1.2)
Thought Problems	0.7 ± 1.2	0.6 ± 1.1	0.0 (−0.2 to 0.3)	0.5 ± 1.2	0.4 ± 0.9	0.1 (−0.2 to 0.4)
Attention Problems	2.7 ± 2.4	3.0 ± 2.5	−0.2 (−0.9 to 0.4)	2.7 ± 2.3	2.8 ± 2.3	−0.1 (−0.7 to 0.5)
Intrusive	3.2 ± 2.9	3.3 ± 2.6	−0.1 (−0.8 to 0.6)	2.6 ± 2.2	3.0 ± 2.6	−0.4 (−1.0 to 0.2)
Aggressive Behavior	4.4 ± 3.7	4.6 ± 4.3	−0.3 (−1.4 to 0.7)	4.8 ± 3.9	4.5 ± 3.6	0.2 (−0.7 to 1.2)
Delinquent Behavior	2.0 ± 2.3	3.1 ± 3.1	−1.1 (−1.8 to −0.4)‡	1.2 ± 1.8	1.8 ± 2.2	−0.6 (−1.1 to −0.1)†
Internalizing	10.5 ± 7.3	11.7 ± 8.1	−1.4 (−3.4 to 0.7)	14.1 ± 9.3	12.2 ± 8.0	1.9 (−0.3 to 4.0)
Externalizing	9.7 ± 7.1	11.1 ± 8.2	−1.5 (−3.6 to 0.5)	8.6 ± 6.1	9.3 ± 6.6	−0.7 (−2.3 to 0.9)
Total Problems	39.1 ± 22.9	43.5 ± 25.3	−5.0 (−11.3 to 1.3)	44.8 ± 26.6	42.7 ± 24.5	2.0 (−4.4 to 8.4)

CI indicates confidence interval. Differences were calculated by subtracting the adjusted mean value for NBW from the adjusted mean value for VLBW subjects. Higher scores indicate poorer functioning.
* Adjusted for sociodemographic status.
† P < .05.
‡ P < .01.

TABLE 3. Rates of Behaviorial Disorder Above Borderline-Clinical Cutoffs*

	Men			Women		
	VLBW	NBW	OR (95% CI)†	VLBW	NBW	OR (95% CI)†
YASR	(n = 116)	(n = 108)		(n = 125)	(n = 124)	
Anxious/Depressed	4 (3%)	9 (8%)	0.4 (0.1–1.3)	12 (10%)	9 (7%)	1.4 (0.6–3.4)
Withdrawn	15 (13%)	10 (9%)	1.4 (0.6–3.2)	17 (14%)	9 (7%)	2.0 (0.8–4.6)
Somatic Complaints	8 (7%)	4 (4%)	1.8 (0.5–6.3)	11 (9%)	5 (4%)	2.3 (0.8–6.7)
Thought Problems	11 (10%)	7 (7%)	1.4 (0.5–3.9)	16 (13%)	10 (8%)	1.6 (0.7–3.8)
Attention Problems	5 (4%)	6 (6%)	0.7 (0.2–2.5)	8 (6%)	8 (7%)	1.0 (0.3–2.7)
Intrusive	8 (7%)	5 (5%)	1.5 (0.5–4.6)	4 (3%)	7 (6%)	0.6 (0.2–1.9)
Aggressive Behavior	10 (9%)	11 (10%)	0.8 (0.3–1.9)	14 (11%)	14 (11%)	1.0 (0.4–2.1)
Delinquent Behavior	4 (3%)	9 (8%)	0.4 (0.1–1.3)	9 (7%)	12 (10%)	0.7 (0.3–1.7)
Internalizing	19 (16%)	23 (21%)	0.7 (0.4–1.4)	37 (30%)	20 (16%)	2.2 (1.2–4.1)‡
Externalizing	24 (21%)	26 (24%)	0.8 (0.4–1.5)	28 (22%)	30 (24%)	0.9 (0.5–1.6)
Total Problems	23 (20%)	27 (25%)	0.7 (0.4–1.3)	33 (26%)	26 (21%)	1.3 (0.7–2.4)
YABCL	(n = 105)	(n = 102)		(n = 119)	(n = 115)	
Anxious/Depressed	10 (10%)	5 (5%)	2.1 (0.7–6.3)	16 (13%)	4 (3%)	4.4 (1.4–13.5)‡
Withdrawn	16 (15%)	6 (6%)	2.8 (1.1–7.5)‡	16 (13%)	8 (7%)	2.1 (0.9–5.1)
Somatic Complaints	7 (7%)	3 (3%)	2.3 (0.6–9.2)	12 (10%)	4 (3%)	3.1 (1.0–10.0)
Thought Problems	13 (12%)	0	19.0 (3.1–∞)§‖	14 (12%)	4 (4%)	3.7 (1.2–11.6)‡
Attention Problems	14 (13%)	6 (6%)	2.5 (0.9–6.7)	21 (18%)	9 (8%)	2.4 (1.0–5.5)‡
Intrusive	7 (7%)	4 (4%)	1.7 (0.5–6.2)	11 (9%)	11 (10%)	1.0 (0.4–2.3)
Aggressive Behavior	11 (11%)	5 (5%)	2.3 (0.8–6.7)	7 (6%)	5 (4%)	1.4 (0.4–4.5)
Delinquent Behavior	16 (15%)	12 (12%)	1.3 (0.6–2.9)	5 (4%)	9 (8%)	0.5 (0.2–1.6)
Internalizing	28 (27%)	19 (19%)	1.6 (0.8–3.1)	34 (28%)	23 (20%)	1.6 (0.9–2.9)
Externalizing	32 (31%)	26 (26%)	1.3 (0.7–2.3)	32 (27%)	29 (25%)	1.1 (0.6–2.0)
Total Problems	48 (46%)	39 (38%)	1.3 (0.8–2.3)	50 (42%)	39 (34%)	1.4 (0.8–2.4)

OR indicates odds ratio.
* Cutoff for Internalizing, Externalizing, and Total Problems = 83rd percentile; for all other scales = 95th percentile.
† Adjusted for sociodemographic status.
‡ P < 0.05.
§ P < 0.001.
‖ OR is a median unbiased estimate from exact logistic regression. Data were insufficient to estimate precisely the upper bound.

ever, parents of the 11 men with neurosensory impairments reported significantly higher mean scores on the intrusive subscale than parents of both the neurologically normal VLBW subjects and of the NBW control subjects (5.3 vs 2.9 vs 2.5, respectively).

When the analyses were performed for singleton births only, the results were similar to the comparisons of the total populations, with the exception that the VLBW singleton men, in addition to reporting fewer delinquent behaviors, reported significantly more anxious/depressed symptoms and fewer internalizing, externalizing, and total behavior problems than their NBW peers. Parents of VLBW singleton men also reported significantly more intrusive symptoms, in addition to more thought problems, than parents of control subjects. VLBW subjects who were born small for gestational age (SGA) did not differ significantly in any of the behavioral subscales from those who were born appropriate for gestational age. The overall results thus were similar when the sub-

TABLE 4. Parent Report on Behavioral Outcomes of VLBW and NBW 20-Year-Old Subjects

YABCL	Men			Women		
	VLBW (Mean ± SD; n = 105)	NBW (Mean ± SD; n = 102)	Mean Difference* (95% CI)	VLBW (Mean ± SD; n = 119)	NBW (Mean ± SD; n = 115)	Mean Difference* (95% CI)
Anxious/Depressed	4.4 ± 4.8	4.1 ± 3.7	0.3 (−0.9 to 1.5)	6.1 ± 6.0	4.2 ± 4.0	1.9 (0.5–3.2)‡
Withdrawn	2.0 ± 2.1	1.5 ± 1.6	0.5 (0–1.0)	2.1 ± 2.2	1.3 ± 1.6	0.8 (0.3–1.3)‡
Somatic Complaints	1.6 ± 2.0	1.4 ± 1.8	0.3 (−0.3 to 0.8)	2.5 ± 2.5	2.2 ± 2.2	0.2 (−0.4 to 0.8)
Thought Problems	0.8 ± 1.6	0.4 ± 0.6	0.4 (0.1–0.7)†	0.8 ± 1.5	0.5 ± 0.9	0.3 (0.0–0.6)
Attention Problems	6.0 ± 5.1	4.9 ± 4.0	1.0 (−0.2 to 2.3)	4.7 ± 4.8	3.4 ± 3.8	1.3 (0.2–2.4)†
Intrusive	3.1 ± 3.0	2.5 ± 2.3	0.6 (−0.1 to 1.3)	2.7 ± 2.8	2.6 ± 2.8	0.1 (−0.6 to 0.8)
Aggressive Behavior	5.4 ± 6.3	4.3 ± 4.8	1.0 (−0.5 to 2.6)	5.0 ± 6.0	4.3 ± 5.3	0.7 (−0.7 to 2.2)
Delinquent Behavior	3.0 ± 4.3	2.8 ± 3.9	0.2 (−0.9 to 1.3)	0.9 ± 1.7	1.4 ± 2.3	−0.5 (−1.0 to 0.1)
Internalizing	6.4 ± 6.3	5.5 ± 4.6	0.8 (−0.7 to 2.3)	8.2 ± 7.8	5.5 ± 5.3	2.7 (1.0–4.4)‡
Externalizing	11.5 ± 12.0	9.5 ± 9.7	1.8 (−1.2 to 4.8)	8.6 ± 9.0	8.3 ± 9.0	0.4 (−1.9 to 2.7)
Total Problems	38.6 ± 30.3	32.7 ± 21.7	5.2 (−1.9 to 12.4)	37.7 ± 29.1	31.1 ± 23.1	6.6 (−0.3 to 13.4)

Differences were calculated by subtracting the adjusted mean value for NBW from the adjusted mean value for VLBW subjects. Higher scores indicate poorer functioning.
* Adjusted for sociodemographic status.
† $P < .05$.
‡ $P < .01$.

jects who were born SGA were excluded from the analyses.

Comparison of VLBW and NBW Women

VLBW women reported significantly more withdrawn behaviors and fewer delinquent behavior problems than their NBW control subjects ($P < .05$; Table 2). Their rates of internalizing behaviors were also higher, with 30% of VLBW versus 16% of control subjects above the borderline clinical cutoff (Table 3). Eighteen percent of VLBW versus 10% of NBW control subjects had rates of internalizing above the clinical cutoff (odds ratio: 2.0 95% confidence interval: 0.9–4.3; data not shown in tables). On the adaptive scales of functioning, VLBW women reported significantly lower scores on excessive alcohol use (2.4 vs 7.0; $P < .01$) and on the Friends (6.7 vs 7.3; $P < .05$) and Family (1.3 vs 1.5; $P < .01$) subscales, ie, fewer friends and poorer family relationships.

Parents of VLBW women reported significantly higher scores on the anxious/depressed, withdrawn, and attention problems subscales for their daughters as well as significantly more overall internalizing problems than parents of control subjects (Table 4). The parent-reported rates of problems above the borderline-clinical cutoff were significantly higher for VLBW women compared with control subjects on the anxious/depressed, thought problems, and attention problems subscales (Table 3). Parent-reported rates of internalizing problems above the borderline-clinical cutoff were 28% versus 20% for VLBW versus NBW women ($P = .13$; Table 3). Twenty-three percent versus 11% were also above the clinical cutoff (odds ratio: 2.4; 95% confidence interval: 1.2–5.0; data not shown in tables).

All of the above-described results were similar after adjusting for IQ in the analyses, with the exceptions that the difference in internalizing problems on the YASR was no longer significant ($P = .11$); neither was the difference in attention problems on the YABCL ($P = .07$) or the rates of attention problems above the borderline-clinical cutoff ($P = .11$). The results also did not differ from the overall results

when subjects with neurosensory impairments were excluded from the analyses, with the exception that the parent report of differences in attention now only bordered on significance ($P = .063$). There were no significant differences in behavior when the 13 VLBW women with neurosensory impairments were compared with the neurologically normal VLBW subjects and with the NBW control subjects.

When the analyses were performed for singleton births only, the results were similar to the overall comparisons, with the exception that VLBW women reported significantly more withdrawn symptoms than their NBW control subjects. When the subjects who were born SGA were excluded from the analyses, the results were similar to the overall outcomes, with the exception that the differences in self-reported internalizing became significant. VLBW subjects who were born SGA reported significantly lower mean scores on the anxious/depressed (7.5 vs 10.9), withdrawn (2.8 vs 4.1), and internalizing subscales (10.2 vs 15.0) and lower rates on the withdrawn subscale (0% vs 17%) than those who were born appropriate for gestational age.

Agreement Between Parent and Young Adult Report of Behavior

Gender-specific Pearson correlations of parent and young adult ratings of young adult problem behavior on the YASR and YABCL ranged from 0.14 to 0.45, within both the VLBW and NBW control populations. The mean parent–young adult agreement of the VLBW populations was lower than that of the control subjects, although not significantly so (0.28 and 0.27 for VLBW men and women, and 0.36 and 0.35 for NBW men and women).

Comparisons of Responses to the ADHD Questionnaire

There were no differences in mean scores on the Inattention, Hyper-Impulsive, or Combined Inattentive/Hyper-Impulsive subtypes of behavior between the young adult VLBW men and women and those of their respective control subjects or in the self-reported rates of the subtypes of ADHD according to

TABLE 5. ADHD Among VLBW and NBW 20-Year-Old Subjects

ADHD Subscales	Self-Report				Parent-Report			
	Men		Women		Men		Women	
	VLBW (n = 115)*	NBW (n = 108)	VLBW (n = 125)	NBW (n = 124)	VLBW (n = 105)	NBW (n = 102)	VLBW (n = 120)†	NBW (n = 115)
Mean scores ± SD								
Inattention	4.6 ± 4	4.8 ± 3	4.2 ± 4	3.8 ± 3	8.3 ± 6	6.4 ± 6‖	5.0 ± 6	4.6 ± 5
Hyper-Impulsive	6.0 ± 5	6.3 ± 4	5.5 ± 4	5.8 ± 4	5.8 ± 6	5.1 ± 5	5.4 ± 6	4.3 ± 4
Combined	10.7 ± 8	11.1 ± 6	9.8 ± 7	9.6 ± 6	14.1 ± 11	11.5 ± 9	10.4 ± 11	9.0 ± 8
Clinical ADHD								
Inattention‡	2 (2%)	1 (1%)	—	1 (1%)	11 (10%)	15 (14%)	16 (13%)	16 (13%)
Hyper-Impulsive‡	—	3 (3%)	5 (4%)	2 (2%)	14 (12%)	9 (8%)	12 (0%)	14 (11%)
Combined§	1 (1%)	—	—	—	8 (7%)	13 (12%)	4 (3%)	2 (2%)

* n = 115 because 1 VLBW male child did not complete the ADHD questionnaire.
† n = 120 because 1 additional parent completed the ADHD female questionnaire.
‡ Number and percentage of subjects who endorsed at least 6 of 9 subscale symptoms.
§ Number and percentage of subjects who endorsed at least 6 of 9 symptoms on both the Inattention and Hyper-Impulsive subscales.
‖ $P < 0.05$.

clinical criteria (Table 5). Parents of VLBW men, however, reported significantly higher mean scores of Inattention for their sons than parents of control subjects but not higher rates of ADHD according to clinical criteria. The higher parent-reported mean inattention scores among VLBW men were no longer significant after adjusting for 20-year IQ and also after excluding subjects with neurosensory impairments or those who were born SGA. The 11 men with neurosensory abnormality, however, had significantly higher scores on the hyper-impulsive subtype of ADHD than both the neurologically normal VLBW and NBW men (10.2 vs 5.3 vs 5.1, respectively). When the analyses were performed for singletons only, the results did not differ from the overall comparisons.

DISCUSSION

This is the first report of the young adult behavioral outcomes and mental health of VLBW children who were beneficiaries of the early years of neonatal intensive care. Our results indicate that the increase in behavioral symptoms reported during childhood persists in adulthood, although the type of problems may differ at this time. VLBW women reported more internalizing problems than control subjects, with significantly higher rates of internalizing problems above the borderline-clinical cutoff. Parents tended to agree with the internalizing symptoms reported by their VLBW daughters by noting significantly more anxious/depressed and withdrawn problems and higher rates of anxious/depressed symptoms above the borderline-clinical cutoff than parents of control subjects, as well as more attention problems. Parents of both VLBW men and women noted significantly more thought problems for their children with significantly higher mean scores on the thought problems subscale among VLBW men and higher rates of thought problems among both VLBW men and women compared with control subjects. Of interest is that both VLBW young men and women reported fewer delinquent behaviors than their NBW control subjects.

The strengths of our study include its relatively large size, gender specificity, and cross-informant parent and child perspective on young adult behavior. Our return rate of 77% of the birth cohort of VLBW subjects compares very favorably with similar longitudinal studies.[46] Our main weakness is the lack of an in-depth psychiatric interview, which would have allowed for the categorization of DSM diagnoses of psychopathology. The relatively small number of VLBW subjects who were born SGA and of those with neurologic abnormality also precludes a true examination of the behavior of these groups as compared with normal VLBW or NBW groups. The lower return rate of the control population and the higher maternal education and higher IQ of those who did participate is in agreement with other studies.[47,48] To control for this bias, we adjusted for sociodemographic status, which includes maternal educational level, in all analyses.

Our primary results are based on the Achenbach young adult self-report and parent questionnaires, which provide a measure of behavioral and emotional problems.[33] Because DSM-IV diagnostic categories of mental disorder have, as yet, not been reported for the YASR and YABCL empirically based syndrome scales, we used Achenbach's suggested cutoffs for the borderline-clinical and clinical ranges of psychopathology to categorize clinical problems. These have been shown to reflect clinical indices of mental health.[36,38,49] We obtained information from both parents and their young adult children because information from different informants may provide different but valid information.[33] The mean correlation of 0.36 between the information obtained from parents of control subjects and their young adult children on the YASR and YABCL is in agreement with the correlation of 0.39 reported by Achenbach for 19- to 22-year-old subjects.[37] Although statistically significant, this relationship indicates that the parent and young adult each contributed a considerable amount of variance not accounted for by the other.[33]

Parents are considered to know their offspring very well into their mid-20s[33] and are considered to be able to contribute valuable information at this age.[50] Achenbach[49] reported that parent ratings on the YABCL generally had a greater association with

concurrent signs of mental health, including suicidal behavior, than did the YASR self-ratings. These findings give credence to the results of our parent reports.

The anxious/depressed syndrome includes items such as "lonely," "cries a lot," "feels worthless," "unhappy," "sad," and "depressed."[33] Our findings of an increase in anxious/depressed and withdrawn symptoms for VLBW women according to parents and increased overall internalizing problems according to both parent and young adult report suggest that VLBW young women may experience significantly higher rates of depression than their NBW peers. In children, the anxious/depressed syndrome of the CBCL has been found to have the closest relationship to depression of the 8 empirically derived syndromes.[51]

Although internalizing behavior is not a measure of depression per se, our finding that 20% of NBW women had internalizing scores above the borderline-clinical cutoff, with 11% above the clinical cutoff, is in agreement with reports that 20% to 25% of young women aged 14 to 26 years have depressive symptoms[52] and with a lifetime prevalence of 21% for 15- to 24-year-old female individuals.[53]

The higher rates of depressive disorders that are prevalent among women in normal populations tend to present after puberty and have been ascribed to hormonal effects and gender-specific sensitivity to factors such as negative life events and chronic psychosocial difficulties, which predispose to depression.[41,54] If extremely low birth weight confers general vulnerability to psychopathology, as suggested by Szatmari et al,[55] then it thus is not surprising that an increase in internalizing symptoms among women becomes evident in young adulthood.

Reports of the childhood and adolescent behavior of VLBW children have mostly stressed the increase in externalizing symptoms and ADHD, which occurs more among male subjects than NBW control subjects.[23–27,55–61] There also have been reports, however, of an increase in depression,[23,25,31,32] anxiety,[31,56] and overall internalizing behaviors, including shy and withdrawn behavior,[29,30,32] among VLBW children. With the exception of the reports of Sykes et al[62] and Botting et al[23], gender-specific differences in internalizing behaviors during childhood have not been reported. Sykes et al[62] noted an increase in parent-reported withdrawn behaviors and internalizing above the clinical cutoff for 7- to 8-year-old VLBW girls, and Botting et al[23] noted an increase in general anxiety but not depression among 12-year-old VLBW girls compared with control subjects. Tideman et al[3] reported a nonsignificant increase in mental health problems among girls who were born at <35 weeks' gestation in a small population of 19-year-old subjects.

We previously reported increased symptoms of hyperactivity in the VLBW cohort at 8 years of age.[35] Our results at 20 years of age reveal an increase in parent reports of attention problems or inattention for VLBW men on the ADHD scale and for VLBW women on the YABCL but not of higher rates of ADHD according to clinical criteria. A decrease in parent-reported rates of hyperactivity[63] and externalizing symptoms[61] between childhood and adolescence has been reported among VLBW and preterm children. In contrast to normal populations, the type of ADHD reported among VLBW children pertains more to symptoms of attention rather than hyperactivity[57] and is less associated with comorbidity such as antisocial and conduct disorder.[23,55,57] This might explain that ADHD in preterm children does not seem to have ominous implications for the persistence of major sequelae into adulthood.[40]

Our lower rates of self-reported delinquency and of excessive alcohol use in both VLBW men and women are in accordance with our previous report of lesser risk taking among VLBW subjects.[1] Saigal et al[25] similarly reported less excessive alcohol use among <1000-g birth weight adolescents at 12 to 16 years of age. There is a paradox in these findings because the lower IQ and school learning problems that occur commonly among VLBW subjects should have predisposed them to more rather than less risk taking and delinquency.[64] We previously postulated that the lower risk taking among VLBW subjects may be attributable to increased parental monitoring,[1,65] although social isolation may also play a role. The results are also consistent with a possible increase in behavioral inhibition in the VLBW subjects, which corresponds to an increased risk of anxiety and depression, as well as decreased antisocial behavior and impulsivity.[66,67]

The clinical significance of the parent-report of an increase in thought problems for VLBW men and higher rates of thought problems for both VLBW men and women compared with their respective control subjects is unclear. An increase in parent-reported thought problems among 8- to 10-year-old <1000-g birth weight children was previously reported in all 4 countries that participated in a multicenter study of preterm behavior.[68] However, the thought problem subscale is one of the shortest on the CBCL, reflects a heterogeneous group of DSM disorders,[69] and requires the most inference from parents, with a high rate of scoring errors.[70] It includes items such as "harms self," "hears things," "sees things," and "has strange ideas," with the YABCL having additional items "can't get mind off thoughts," "repeats acts," and "strange behavior." van Os and colleagues[71–73] suggested that psychotic symptoms, which are most prevalent among young adults, occur on a continuum that extends from normality through depressive states to schizophrenia. An association between schizophrenia and low birth weight has been suggested from epidemiologic studies, but it is unclear whether this pertains to low birth weight resulting from intrauterine growth failure, prematurity, or both.[4,11–13,74,75] In an abstract, Rifkin et al[76] reported 2 cases of schizophrenia among 60 VLBW young adults. We found no cases of schizophrenia at 20 years of age, but 5 VLBW subjects had a history of bipolar disorder.[1] Schizophrenia and bipolar disorder both have a prevalence of ~1% in adult populations, with an average age of onset of schizophrenia of 18 to 25 years for men and 25 to 35 years for women.[77] Even if additional cases become

evident on longer in-depth follow-up, our relatively small population and thus low statistical power hinder any conclusion in this regard.

In summary, our results suggest significantly more psychopathology among VLBW young adults than among control subjects, including internalizing symptoms among women and possible thought problems among both men and women. It will be important to follow the subjects into mature adulthood to evaluate whether the 20-year findings persist and are predictive of increased psychopathology defined according to DSM diagnoses. Evidence, to date, indicates the need for an increased awareness of the possibility that psychologic problems may present among VLBW survivors in the postpubertal years and the need for anticipatory guidance and early intervention that might help to prevent or ameliorate these problems.[78–80]

REFERENCES

1. Hack M, Flannery D, Schluchter M, Cartar L, Borowski E, Klein N. Young adult outcomes of very low birth weight children (VLBW, < 1.5 kg). *N Engl J Med.* 2002;346:149–157
2. Pharoah POD, Stevenson CJ, West CR. General certificate of secondary education performance in very low birthweight infants. *Arch Dis Child.* 2003;88:295–298
3. Tideman E, Ley D, Bjerre I, Forslund M. Longitudinal follow-up of children born preterm: somatic and mental health, self-esteem and quality of life at age 19. *Early Hum Dev.* 2001;61:97–110
4. Cannon M, Jones PB, Murray RM. Obstetric complications and schizophrenia: historical and meta-analytic review. *Am J Psychiatry.* 2002;159:1080–1092
5. Done DJ, Johnstone EC, Frith CD, Golding J, Shepherd PM, Crow TJ. Complications of pregnancy and delivery in relation to psychosis in adult life: data from the British perinatal mortality survey sample. *BMJ.* 1991;302:1576–1580
6. Brown AS, van Os J, Driessens C, Hoek H, Susser ES. Further evidence of relation between prenatal famine and major affective disorder. *Am J Psychiatry.* 2000;157:190–195
7. Buka SL, Fan AP. Association of prenatal and perinatal complications with subsequent bipolar disorder and schizophrenia. *Schizophrenia Res.* 1999;39:113–119
8. Hodgins S, Kratzer L, McNeil T. Obstetric complications, parenting, and risk of criminal behavior. *Arch Gen Psychiatry.* 2001;58:746–752
9. Tibbetts SG, Piquero AR. The influence of gender, low birth weight, and disadvantaged environment in predicting early onset of offending: a test of Moffit's interactional hypothesis. *Criminology.* 1999;37:843–877
10. Susser ES, Lin SP. Schizophrenia after prenatal exposure to the Dutch hunger winter of 1944–1945. *Arch Gen Psychiatry.* 1992;49:983–988
11. Wahlbeck K, Forsen T, Osmond C, Barker DJP, Eriksson JG. Association of schizophrenia with low maternal body mass index, small size at birth, and thinness during childhood. *Arch Gen Psychiatry.* 2001;58: 48–52
12. Jones PB, Rantakallio P, Hartikainen A-L, Isohanni M, Sipila P. Schizophrenia as a long-term outcome of pregnancy, delivery, and perinatal complications: a 28-year follow-up of the 1966 North Finland general population birth cohort. *Am J Psychiatry.* 1998;155:355–364
13. McNeil TF, Cantor-Graae E, Cardenal S. Prenatal cerebral development in individuals at genetic risk for psychosis: head size at birth in offspring of women with schizophrenia. *Schizophrenia Res.* 1993;10:1–5
14. Dalman C, Thomas HV, David AS, Gentz J, Lewis G, Allebeck P. Signs of asphyxia at birth and risk of schizophrenia. *Br J Psychiatry.* 2001;179: 403–408
15. van Os J, Jones P, Lewis G, Wadsworth M, Murray R. Developmental precursors of affective illness in a general population birth cohort. *Arch Gen Psychiatry.* 1997;54:625–631
16. Richards M, Maughan B, Hardy R, Hall I, Strydom A, Wadsworth M. Long-term affective disorder in people with mild learning disability. *Br J Psychiatry.* 2001;179:523–527
17. Sigurdsson E, van Os J, Fombonne E. Are impaired childhood motor skills a risk factor for adolescent anxiety? Results from the 1958 U.K. birth cohort and the National Child Development study. *Am J Psychiatry.* 2002;159:1044–1046
18. Pine D, Shaffer D, Schonfeld IS. Persistent emotional disorder in children with neurological soft signs. *J Am Acad Child Adolesc Psychiatry.* 1993;32:1229–1236
19. Cohen P, Pine DS, Must A, Kasen S, Brook J. Prospective associations between somatic illness and mental illness from childhood to adulthood. *Am J Epidemiol.* 1998;147:232–239
20. Ortega AN, Huertas SE, Canino G, Ramirez R, Rubio-Stipec M. Childhood asthma, chronic illness, and psychiatric disorders. *J Nerv Ment Dis.* 2002;190:275–281
21. Bennett DS. Depression among children with chronic medical problems: a meta-analysis. *J Pediatr Psychol.* 1994;19:149–169
22. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS. Cognitive and behavioral outcomes of school-aged children who were born preterm. A meta-analysis. *JAMA.* 2002;288:728–737
23. Botting N, Powls A, Cooke RWI, Marlow N. Attention deficit hyperactivity disorders and other psychiatric outcomes in very low birthweight children at 12 years. *J Child Psychol Psychiatry.* 1997;38:931–941
24. Whitaker AH, Van Rossem R, Feldman JF, et al. Psychiatric outcomes in low-birth-weight children at age 6 years: relation to neonatal cranial ultrasound abnormalities. *Arch Gen Psychiatry.* 1997;54:847–856
25. Saigal S, Pinelli J, Hoult L, Kim MM, Boyle M. Psychopathology and social competencies of adolescents who were extremely low birth weight. *Pediatrics.* 2003;111:969–975
26. McCormick MC, Brooks-Gunn J, Workman-Daniels K, Turner J, Peckham GJ. The health and developmental status of very low-birth-weight children at school age. *JAMA.* 1992;267:2204–2208
27. Breslau N, Klein N, Allen L. Very low birthweight: behavioral sequelae at nine years of age. *J Am Acad Child Adolesc Psychiatry.* 1988;27:605–612
28. Taylor HG, Hack M, Klein N. Attention deficits in children with < 750 gram birthweight. *Child Neuropsychol.* 1998;4:21–34
29. Nadeau L, Boivin M, Tessier R, Lefebvre F, Robaey P. Mediators of behavioral problems in 7-year-old children born after 24 to 28 weeks of gestation. *J Dev Behav Pediatr.* 2001;22:1–10
30. Weisglas-Kuperus N, Koot HM, Baerts W, Fetter WPF, Sauer PJJ. Behavior problems of very low-birthweight children. *Dev Med Child Neurol.* 1993;35:406–416
31. Levy-Shiff R, Einat G, Har-Even D, et al. Emotional and behavioral adjustment in children born prematurely. *J Clin Child Psychol.* 1994;23: 323–333
32. Hoy EA, Sykes DH, Bill JM, Halliday HL, McClure BG, McReid M. The social competence of very-low-birthweight children: teacher, peer, and self-perceptions. *J Abnorm Child Psychol.* 1992;20:123–150
33. Achenbach TM. *Manual for the Young Adult Self-Report and Young Adult Behavior Checklist.* Burlington, VT: University of Vermont; 1997
34. Hobel CJ, Hyvarinen M, Okada DM, Oh W. Prenatal and intrapartum high-risk screening I. Prediction of the high-risk neonate. *Am J Obstet Gynecol.* 1973;117:1–9
35. Hack M, Breslau N, Aram D, Weissman B, Klein N, Borawski-Clark E. The effect of very low birth weight and social risk on neurocognitive abilities at school age. *J Dev Behav Pediatr.* 1992;13:412–420
36. Ferdinand RF, Verhulst FC. The prediction of poor outcome in young adults: comparison of the Young Adult Self-Report, the General Health Questionnaire and the Symptom Checklist. *Acta Psychiatr Scand.* 1994; 89:405–410
37. Achenbach TM, Howell CT, McConaughy SH, Stanger C. Six-year predictors of problems in a national sample: III. Transitions to young adult syndromes. *J Am Acad Child Adolesc Psychiatry.* 1995;34:658–669
38. Wiznitzer M, Verhulst FC, van den Brink W, Koeter M, Van der Ende J, Giel R, Koot HM. Detecting psychopathology in young adults: the Young Adult Self Report, the General Health Questionnaire and the Symptom Checklist as screening instruments. *Acta Psychiatr Scand.* 1992; 86:32–37
39. Barkley RA, Murphy KR. *Attention Deficit Hyperactivity Disorder: A Clinical Workbook.* New York, NY: Guilford Press; 1998
40. Murphy KR, Barkley RA, Bush T. Young adults with attention deficit hyperactivity disorder: subtype differences in comorbidity, educational, and clinical history. *J Nerv Ment Dis.* 2002;190:147–157

41. Cyranowski JM, Frank E, Young E, Shear K. Adolescent onset of the gender difference in lifetime rates of major depression. *Arch Gen Psychiatry*. 2000;57:21–27

42. Hankin BL, Abramsom LY, Moffitt TE, Silva PA, McGee R, Angell KE. Development of depression from preadolescence to young adulthood: emerging gender differences in a 10-year longitudinal study. *J Abnorm Psychol*. 1998;107:128–140

43. Johnson JG, Cohen P, Dohrenwend BP, Link BG. A longitudinal investigation of social causation and social selection processes involved in the association between socioeconomic status and psychiatric disorders. *J Abnorm Psychol*. 1999;108:490–499

44. Rutter M, Tizard J, Whitmore K. *Education, Health and Behaviour*. London, United Kingdom: Longman Group; 1970

45. Wechsler D. *The Wechsler Adult Intelligence Scale-Revised*. San Antonio, TX: The Psychological Corporation; 1981

46. Strauss RS. Adult functional outcome of those born small for gestational age. Twenty-six year follow-up of the 1970 British birth cohort. *JAMA*. 2000;283:625–632

47. Aylward GP, Hatcher RP, Stripp B, Gustafson NF, Leavitt A. Who goes and who stays: subject loss in a multicenter, longitudinal follow-up study. *Dev Behav Pediatr*. 1985;6:3–8

48. Wolke D, Sohne B, Ohrt B, Riegel K. Follow-up of preterm children: important to document dropouts. *Lancet*. 1995;345:447

49. Achenbach TM, Howell CT, McConaughy SH, Stanger C. Six-year predictors of problems in a national sample: IV. Young adults signs of disturbance. *J Am Acad Child Adolesc Psychiatry*. 1998;37:718–727

50. Visser JH, Van der Ende J, Koot HM, Verhulst FC. Predictors of psychopathology in young adults referred to mental health services in childhood or adolescence. *Br J Psychiatry*. 2000;177:59–65

51. Compas BE, Oppedisano G, Connor JK, Gerhardt CA, Hinden BR, Achenbach TM. Gender differences in depressive symptoms in adolescence: comparison of national samples of clinically referred and nonreferred youths. *J Consult Clin Psychol*. 1997;65:617–626

52. Rickert VI, Wiemann CM, Berenson AB. Ethnic differences in depressive symptomatology among young women. *Obstet Gynecol*. 2000;95:55–60

53. Blazer DG, Kessler RC, McGonagle KA, Swartz MS. The prevalence and distribution of major depression in a national community sample: the National Comorbidity Survey. *Am J Psychiatry*. 1994;151:979–986

54. Ge X, Lorenz F, Conger RD, Elder GH Jr, Simons RL. Trajectories of stressful life events and depressive symptoms during adolescence. *Dev Psychol*. 1994;30:467–483

55. Szatmari P, Saigal S, Rosenbaum P, Campbell D. Psychopathology and adaptive functioning among extremely low birthweight children at eight years of age. *Dev Psychopathol*. 1993;5:345–357

56. Horwood LJ, Mogridge N, Darlow BA. Cognitive, educational, and behavioral outcomes at 7 and 8 years in a national very low birthweight cohort. *Arch Dis Child Fetal Neonatal Ed*. 1997;79:F12–F20

57. Elgen I, Sommerfelt K, Markstad T. Population based, controlled study of behavioural problems and psychiatric disorders in low birthweight children at 11 years of age. *Arch Dis Child Fetal Neonatal Ed*. 2002;87:F128–F132

58. Pharoah POD, Stevenson CJ, Cooke RWI, Stevenson RC. Prevalence of behaviour disorders in low birthweight infants. *Arch Dis Child*. 1994;70:271–274

59. Rose SA, Feldman JF, Rose SL, Wallace IF, McCarton C. Behavior problems at 3 and 6 years: prevalence and continuity in full-terms and preterms. *Dev Psychopathol*. 1992;4:361–374

60. Ross G, Lipper EG, Auld PAM. Social competence and behavior problems in premature children at school age. *Pediatrics*. 1990;86:391–397

61. Schothorst PF, van Engeland H. Long-term behavioral sequelae of prematurity. *J Am Acad Child Adolesc Psychiatry*. 1996;35:175–183

62. Sykes DH, Hoy EA, Bill JM, McClure BG, Halliday HL, Reid MM. Behavioural adjustment in school of very low birthweight children. *J Child Psychol Psychiatry*. 1997;38:315–325

63. Stevenson CJ, Blackburn P, Pharoah POD. Longitudinal study of behaviour disorders in low birthweight infants. *Arch Dis Child Fetal Neonatal Ed*. 1999;81:F5–F9

64. Kandel DB, Davies M. High school students who use crack and other drugs. *Arch Gen Psychiatry*. 1996;53:71–80

65. Chilcoat HD, Breslau N. Pathways from ADHD to early drug use. *J Am Acad Child Adolesc Psychiatry*. 1999;38:1347–1354

66. Carver CS, White TL. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS Scales. *J Pers Soc Psychol*. 1994;67:319–333

67. Depue RA, Lenzenweger MF. A Neurobehavioral Dimensional Model. Handbook of Personality Disorders. Theory, Research, and Treatment. New York, NY: Guilford; 2001:136–176

68. Hille ETM, den Ouden AL, Saigal S, et al. Behavioural problems in children who weigh 1000 g or less at birth in four countries. *Lancet*. 2001;357:1641–1643

69. Lengua LJ, Sadowski CA, Friedrich WN, Fisher J. Rationally and empirically derived dimensions of children's symptomatology: expert ratings and confirmatory factor analyses. *J Consult Clin Psychol*. 2001;69:683–698

70. Drotar D, Stein REK, Perrin EC. Methodological issues in using the Child Behavior Checklist and its related instruments in clinical and child psychology research. *J Clin Child Psychol*. 1995;184–192

71. van Os J, Verdoux H, Maurice-Tison S, Gay B, Liraud F, Salamon R, Bourgeois M. Self-reported psychosis-like symptoms and the continuum of psychosis. *Soc Psychiatry Psychiatr Epidemiol*. 1999;34:459–463

72. Verdoux H, van Os J. Psychotic symptoms in non-clinical populations and the continuum of psychosis. *Schizophrenia Res*. 2002;54:59–65

73. Johns LC, van Os J. The continuity of psychotic experiences in the general population. *Clin Psychol Rev*. 2001;21:1125–1141

74. Kendell RE, McInneny K, Juszczak E, Bain M. Obstetric complications and schizophrenia. *Br J Psychiatry*. 2000;174:514–522

75. Rifkin L, Lewis S, Jones P, Toone B, Murray R. Low birth weight and schizophrenia. *Br J Psychiatry*. 1994;165:357–362

76. Rifkin L, Lewis SW, Townsend J, Stewart A. Schizophrenia and very low birthweight. *Schizophrenia Res*. 2000;11:94

77. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. *Arch Gen Psychiatry*. 1994;51:8–19

78. Beardslee WR, Gladstone TRG, Wright EJ, Cooper AB. A family-based approach to the prevention of depressive symptoms in children at risk: evidence of parental and child change. *Pediatrics*. 2003;112(2). Available at: www.pediatrics.org/cgi/content/full/112/2/e11a

79. Deckard-Deater K, Bulkley J. Parent concerns in long-term follow-up. *Semin Neonatol*. 2000;5:171–178

80. Laucht M, Esser G, Schmidt MH. Differential development of infants at risk for psychopathology: the moderating role of early maternal responsivity. *Dev Med Child Neurol*. 2001;43:292–300

81. Usher R, McLean F. Intrauterine growth of live-born Caucasian infants at sea level: standards obtained from measurements in 7 dimensions of infants born between 25 and 44 weeks of gestation. *Pediatrics*. 1969;74:901–910